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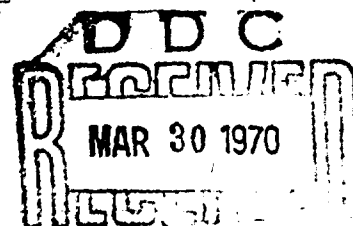
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Deutsche Medicinische Wochenschrift  
No. 49  
December 4, 1890

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GERMAN  
MEDICAL WEEKLY

Taking into account the German Medical Practices of Official Reports,  
Public Health Care and the Interests of the Medical Profession.

Founded by Dr. Paul Borner  
Sixteenth Year

Editor and Health Advisor--Dr. S. Guttman in Berlin W.

Published by Georg Thieme, Leipzig-Berlin.

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I. From the Hygienic Institute of Herr Geheimtath Koch in Berlin

On the Occurrence of Diphtheria-Immunity and Tetanus Immunity in Animals.

By Staff Doctor Dr. Behring, Assistant at the Institute,  
and Dr. Kitasato of Tokyo.

In our long-continued studies we have come closer to understanding the therapeutical and immunization problems of diphtheria (Behring) and tetanus (Kitasato), and we have succeeded in curing both of these infectious diseases not only in infected animals, but also in pre-treating animals in such a way so that they will no longer be susceptible to either diphtheria or tetanus.

We shall discuss the basis<sup>1</sup> for developing the cure and immunization of animals only insofar as it is necessary to prove the validity of the following paragraph:

\*The immunity of rabbits and mice, which are immunized against tetanus, is based on the capacity of the cell-free blood fluid to render harmless the toxic substances produced by the tetanus bacilli.<sup>1</sup>

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<sup>1</sup>More exact reports on this subject will follow in the Zeitschrift fur Hygiene (Magazine for Hygiene).

The explanation for the immunity, which is expressed in the above paragraph, has not been taken into consideration in those works that have been carried out most recently on the subject of immunity.

Aside from the phagocytosis theory, which seeks the explanation in the vital activity of the cells, the anti-bacterial effect of the blood and the becoming use to the poison of the animal organism were also taken into account.

If one of the explanative principles were not sufficient or were recognized as false by one of the authors involved in the experiments, then one, by the process of elimination, was forced to search for other theories. Bouchard said this in his speech delivered at the X International Medical Congress, which restated most forcefully the previous position of the immunity problem as follows: "We therefore no longer speak of the leucocytes and of the nervous cells becoming used to the poisonous bacteria: this is now sheer rhetoric" and: "This is, in effect, the bacterial state that constitutes the vaccine or develops the immunity."

This positive explanation is actually the same as what Roger<sup>2</sup> expressed earlier with the words: "The vaccination determines in the organism some chemical modifications that render the body fluids and the tissues unfavorable to the growth of the microbe against which one protects the animals."

Behring, in his studies with diphtheria immunized rats and immunized guinea pigs stated that none of the above-mentioned theories was capable of explaining the immunity of these animals, and he realized that it was necessary to search for another explanative principle. After many unsuccessful efforts, a new possible explanative principle was seen in the destructive qualities of the diphtheria-toxic in the diphtheria-immunized animals in which the immunization for diphtheria. In the application of experiments made with diphtheria we succeeded in obtaining results, which, as far as we can recognize, are clearly conclusive.

The following experiments proved that:

1. The blood of the tetanus-immunized rabbits has qualities to destroy the tetanus poison.
2. These qualities can be found in the extra-vascular blood as well as in the cell-free serum taken out of the blood.
3. These qualities are of such a permanent nature that they remain effective also in the organism of other animals so that one is able to attain outstanding therapeutical effects through blood and serum transfusions.
4. The anti-tetanus poisons are not found in the blood of animals that are not immunized against tetanus, and if one does not [here a piece of the page is torn out of the original] can be found after the death of the animal and in its remaining fluids.

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<sup>2</sup>"Contribution to the Study of Acquired Immunity." 1890.

We offer as proof for these assumptions the following test series:

In one series, which will be described more precisely later<sup>1</sup>, a rabbit was immunized against tetanus. In testing the degree of immunity, 10 ccm of a germ containing a virulent tetanus bacilli-culture was injected, of which 0.5 ccm is sufficient in a normal rabbit to destroy entirely the tetanus in the same rabbit. Each rabbit, however, remained completely healthy.

The same rabbits, however, became immunized not only against infection with live tetanus bacilli, but also were immunized against the tetanus poison; for they endured 20 times of the same amount of poison without any damage, which is sufficient to kill normal rabbits without exception.<sup>2</sup>

The poison was taken out of these rabbits from the carotid blood.

A mouse was infected with 0.2 ccm of this serum in liquid blood before clotting, and another was infected in the stomach cavity with 0.5 ccm. Both were vaccinated with a virulent tetanus bacilli along with 2 control mice after 24 hours and indeed so strongly that the control animals caught tetanus within 20 hours and died 36 hours later. Both of the pre-treated mice, on the other hand, remained permanently healthy.

The larger amount of blood was set aside until the rich serum had settled.

Six mice were injected with 0.2 ccm of this serum in the stomach cavity; 24 hours later infection occurred, but all six remained healthy, whereas the control mice died of tetanus in less than 48 hours.

In addition, other therapeutical successes can be attained with the serum if one first infects the animal and then injects the serum afterwards into the stomach cavity.

Moreover, we have arranged with serum tests that are capable of illustrating its great anti-poisonous effect.

From a 10-day-old tetanus culture, which was kept germ free by means of filters, 0.00005 ccm was sufficient to kill the same mouse in less than two days.

We then mixed 5 ccm of serum from the tetanus-immunized rabbits with 1 ccm of this culture, and we let the serum take its effect on the tetanus poison contained in the culture. From this mixture 4 mice received 0.2 ccm each, i.e., 0.033 ccm culture, or more than 300 times the dosage otherwise deadly for mice; all the 4 mice remained permanently healthy: on the other hand, the control mice died after 36 hours from 0.0001 of the culture.

All the mice from the previous listed test series and all those that had been injected with the serum in the stomach cavity as well as those injected with the mixture of tetanus poison remained permanently immunized.

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<sup>1</sup>In a work that soon appeared in the Zeitschrift fur Hygiene: On the Qualities of the Tetanus Poison, from Kitasato.

<sup>2</sup>Area of the page where this footnote is placed is so badly torn that it is illegible.

so far as it has been observed. They later repeated once again the vaccination with virulent tetanus bacilli; again no trace of the disease occurred.

The fact is therefore especially noteworthy because in innumerable separate experiments not one mouse, not one rabbit, in fact, not one animal at all ever tested was found to be tetanus-immunized, and because the tests that were conducted over a long period of time in this hygienic institute to immunize one of the previously known kinds of animals against tetanus had been thoroughly unsuccessful.

We may therefore rightly conclude that the above-mentioned concept on the developing of immunity is clearly a harmless immunity method which may be carried out immediately and without any difficulty, and one that would also satisfy an extensive rationalization of the blood and serum. Of course control experiments were also conducted with the blood and serum of non-immunized rabbits; the blood and serum showed therapeutically, as well as in relationship to influencing the tetanus poison, as totally ineffective.

Special tests have also shown that the same is true of cattle, calves, horses, and sheep serum.

Even the blood inside the vessels of living non-immunized animals have no anti-tetanus poison qualities as the following tests, which were repeated many times, have indicated:

Rabbits, which have been injected subcutaneously with 0.5 ccm of poisonous germ-free tetanus cultures, die in 5 or 6 days with the typical tetanus symptoms. A serum transudation is found almost without exception in the pectoral cavity when dissecting.

On the average 0.3 ccm of this transudation is sufficient to make a mouse ill and die and the same dosage is sufficient to cause the tetanus to re-occur in the blood of the tetanus-poisoned mice.

From our results we drew conclusions which, since they have already proved successful for the discovery of therapeutically effective means in animals, might also prove useful for the treating of men suffering from diphtheria and tetanus.

In conclusion we would like very much to make one thing clear.

In earlier times, blood transfusions were considered to be an heroic and at certain times an exceedingly effective method of healing; today, however, one feels the same can be performed with a physiological cooking salt solution. With this in mind our test results stress the importance of the saying: "Blood is a very special fluid".